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## PART 1.—ORIGINAL ARTICLES.

*The Amok of the Malays.* By W. GILMORE ELLIS, M.D.,  
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Singapore.

We are all of us familiar with the expression “to run amuck,” but perhaps comparatively few of us are familiar with the significance of the term in the Eastern Archipelago. Amuck, or, as it is properly spelt *Amok*, is a Malay word, and means a furious assault, its derivatives, *Mengamok* and *Pen-gamok* respectively, meaning to commit a furious assault and the person who runs Amok.

A Malay who runs Amok is always in a state of furious homicidal passion, and runs armed through the most crowded street or village stabbing right and left at man, woman, or child, relation, friend, or stranger.

For the convenience of this paper I shall call the man who runs Amok an “Amoker,” and the crime “Amoking.”

It is necessary to state at once that I do not in any way intend to discuss the point as to whether the judicial execution of men Amoking is right or wrong, or as to whether execution of all Amokers would tend to lessen the frequency of the crime. I believe Penang has claimed that the Chief Justice’s (Sir Wm. Norris) sentence, which reads like one of those of the middle ages, and which I will give in detail later on, passed upon an Amoker, and carried out within eight days of the Amok in 1846, was the means of stamping out Amok entirely for years, but I can obtain no reliable information in proof of this. I intend trying to give a brief sketch of Amok and its causes, some notes on recent cases, and to point out a possible field in which its pathology may eventually be determined.

Athenian Asylum, although many chronic cases were admitted in the first six months, from October, 1887, to April, 1888, yet the results have been widely different from those in Corfu. The whole number of admissions from October, 1887, to January, 1893, was 361, covering, I suppose, about 350 different persons. Of these 361 there had been discharged up to January 1st, 1893, 245, of whom 66 had recovered and 57 had died, leaving 116 then under treatment. This shows a preponderance of recoveries over deaths, which would have been considerably greater but for the number of deaths from general paralysis; these have been about 15 in the five years, I believe. Of the comparative prevalence of this fatal malady in Corfu and at Athens, Dr. Chirigotes said in his first report (up to January 1st, 1889) that there were not so many cases of general paralysis among his 400 patients in Corfu, during the ten years 1877-1886, as among the 88 cases received at the Athenian Asylum in its first 15 months.

With these imperfect observations, which may, perhaps, lead others more competent to write on the interesting subject of insanity in Greece, I submit the matter to the readers of the "Journal of Mental Science."

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*The Treatment of Myxœdema and Cretinism, being a Review of the Treatment of these Diseases with the Thyroid Gland, with a Table of 100 Published Cases.\** By CECIL F. BEADLES, M.R.C.S., L.R.C.P., Assistant Medical Officer, Colney Hatch Asylum.

### *Introductory.*

I propose in the following paper to review briefly the treatment that has recently been made use of in myxœdema, and compare the several ways in which it has been carried out, after a few preliminary remarks on the pre-thyroid methods.

First let me note that myxœdema, although not common, is now known not to be so rare a disease as was supposed only a few years back. During the past five years, that is to say from the year 1888, when the profession was more generally

\* The most important discussions that have yet taken place are those at Nottingham in July, 1892 (in the early days of the new thyroid treatment), and Edinburgh, February 15th and 16th, 1893. To the reports of these I would direct your attention. I understand that at the annual meeting of the British Medical Association, at Newcastle, in August next, Prof. Horsley has promised to open a discussion on "The Thyroid."

awakened to the existence of this disease by the Clinical Society's report, up to the present time a careful search reveals just 200 distinct cases\* referred to in the various medical journals of this country. But the vast majority of cases go unrecorded, for until within the last eighteen months cases were seldom reported unless there was something of particular interest in the symptoms of the case, or some point in the pathology of the disease that was thought worthy of notice.

*The Older or pre-Thyroid Methods of Treatment.*

From the time Sir William Gull† in 1873 first called attention to the disease now known under the name of myxœdema,‡ up to July, 1891, when Dr. George Murray read his paper in the Section of Therapeutics of the British Medical Association, at Bournemouth, entitled "Note on the Treatment of Myxœdema by Hypodermic Injections of an Extract of the Thyroid Gland of a Sheep," no treatment was known that could be said to have anything but the slightest influence on this slowly progressive disease, much less cure it. Since Dr. Murray's valuable suggestion, however, I think we may say that we now have in our possession a substance which can produce a greater change in persons suffering from myxœdema than is the case with any single drug or any other known disease.

During the time above-mentioned most of the preparations in the pharmacopœia, as well as others not contained therein, had been tried with a singularly unfavourable result. There was only one drug known that appeared to exercise any notable influence for the better. This was jaborandi.

Of the 65 out of the 109 cases of myxœdema reported on by the Committee of the Clinical Society§ in which the form of treatment adopted was specified, this was the only drug mentioned that seemed to be followed by a slight improvement. It was made use of in eighteen of the cases. This result was the same as that which has since been observed, and the result was similar in a patient I had under my care in Colney Hatch Asylum|| in the early part of 1892, where she had been an

\* These include 40 cases referred to at the Edinburgh Med.-Chir. Soc. on February 15th and 16th, 1893, but not the 50 cases which were then mentioned as known to exist about the neighbourhoods of Edinburgh and Dundee.

† "On a Cretinoid State supervening in Adult Life in Women," Clin. Soc. of London, 1873.

‡ "Ord. Medico-Chir. Trans.," Vol. lxi., p. 57, 1877.

§ "Report of a Committee of the Clinical Society of London to investigate the subject of Myxœdema," 1888.

|| Case reported in "The Journal of Path. and Bact.," No. 2, 1892.

inmate over seven years. Although a slight improvement at times appeared to follow the administration of jaborandi, it was only very transitory, with but a slight noticeable change either in the bodily or mental symptoms, and the patient rapidly relapsed into her former condition.

Myxœdema is naturally a very chronic disease, in which periods of abatement are wont to occur, and, as is well known, myxœdematous patients under no special treatment vary greatly from time to time, but especially so with change of temperature and the season of the year; but although they feel in better health and are more active when the weather is warm, they never lose the characteristic facial aspect, although it may to a slight degree diminish. I have never heard of a patient who has so far recovered that it has been impossible to diagnose the case as one of myxœdema. They are always worse in the winter months, and it is then that death almost invariably takes place. Some of the improvement that has been said to occur after the use of jaborandi may therefore depend on the patient's surroundings, and it should be stated in which months this has taken place—a point which has not always been noted, and has, therefore, tended to somewhat mislead as to the benefit derived from this medicine.

Dr William Ord\* at one time went so far as to state that in a few cases "under the prolonged use of jaborandi the signs of myxœdema have almost disappeared." But even this is by no means the rule, and only the other day Dr. Ord remarked at the Clinical Society† that "two years ago the disease was regarded as incurable."

The Committee appointed by the Clinical Society in their classical work on myxœdema already referred to, in their general summary of treatment, say:—"The use of tonics, particularly of iron, quinine, and hypophosphites (meeting the obvious debility belonging to the disease) has been adopted with a certain amount of temporary success. Having regard to the defective action of the skin, Jaborandi and pilocarpin have in many cases been administered, and, when administered over long periods, have appeared to exercise much beneficial influence. Nitro-glycerine has been used in a very limited number of cases with fairly good results. An important element in the treatment is the maintenance of warmth in the surrounding atmosphere, and the regular removal of patients during the winter to southern climates has appeared to mitigate

\* Quain's "Dictionary of Medicine," 1883, p. 1016.

† "Brit. Med. Journ.," February 4th, 1893, p. 252.

their sufferings and to prolong their tenure of life.”\* On another page† they enter more fully into the results reported of individual drugs.

Other drugs appear to be of even less value, and the same remarks apply as those just made with regard to jaborandi. Of the drugs which have had special attention called to them and been stated at various times to have been used beneficially may be mentioned nux vomica, strychnia, arsenic and iron, and nitro-glycerine, by the use of which drugs, when combined with careful diet, baths, and massage, Sir Andrew Clark “regards the disease as fairly curable.”‡ This is a vague term, and few would hold that there is even a “temporary cure” by these means.§ There are few illustrations on record. Dr. McCall Anderson, of Glasgow, has lately published a case || of a female, 20 years of age, with myxædema of one year duration. The treatment consisted of taking arsenic and strychnine internally with a shampoo daily for half-an-hour, and an occasional vapour bath, in addition to which every now and then she had a subcutaneous injection of pilocarpine, gr.  $\frac{1}{4}$ , and a hot electric bath for half-an-hour at a time. A change for the better commenced after ten days, and in three months’ time “great improvement was manifest.” This, of course was an early case; the mind was not impaired. In another case, of longer duration, which he publishes at the same time, similar treatment produced no result after continuation for two months; it was then combined with the administration of thyroid juice, and was followed by marked improvement. I shall, however, refer to this case again.

Dr. A. Morison, at a meeting of the Pathological Society on October 18, said “he had seen a great benefit follow systematic

\* “Myxædema Report,” p. 34.

† This is as follows :—“Jaborandi in 12 and pilocarpin in six. Of these 18, 11 improved. In three improvement was great, and in one of these hot-air baths were also used. In five no improvement; in two results not stated. Nitro-glycerine in three. Marked temporary improvement in one, slight improvement in one, no effect in one. Iron, quinine, and sulphur baths caused almost entire disappearance of œdema in one. Iodide of potassium in large doses temporarily relieved occipital headache in one. Induced current in two. Improvement in one. Galvanism to the spine probably of use in one. Iron beneficial in four, but in a much larger proportion no good resulted. Strychnia or nux vomica in 10. Improvement in two. Quinine, hydrobromic acid, phosphorus, cod-liver oil, cold baths, milk diet, and ‘tonics’ apparently useless.” The above are extracted from 65 answers received. See page 22 of report.

‡ Quain’s “Dictionary of Medicine,” 1883.

§ Dr. Affleck (“Edin. Med. Jour.,” May, 1893, p. 1050) has, however, known great improvement to follow this treatment.

|| “The Practitioner,” January, 1893.

massage; the patient improved for a time, but ultimately the massage lost its apparent effect and a fatal result ensued.\* Other observers have noted precisely the same fact.

Dr. William Dyson, in recording a case of myxœdema in a male who was under his care at the Sheffield General Infirmary,† writes, "On the whole the drug treatment did not appear to do much good; I was inclined to attribute this general improvement to the warmth, excellent nursing, and good wholesome food which he received." A photograph reproduced, which was taken when he was at his best, shows, however, an undoubted well-marked case of myxœdema. With this remark of Dr. Dyson many will agree.

Dr. Hector Mackenzie, lately in a lecture on the recent advances in the treatment of myxœdema, when speaking of a certain case that he has since treated by thyroid extract, said: "During the two years and a half we had been watching the patient the disease had been slowly, but steadily, progressing. Whether our treatment by jaborandi, tonics, rest in bed, massage, and the other means we had employed had prevented a more rapid progress we cannot say. Certainly, she had been temporarily benefited a little by her two admissions, and she herself had some faith in the efficacy of the medicines prescribed for her."‡

Dr. Hermon Gordinier read a paper last year before the Medical Society of New York, in which he said of a female with myxœdema of two years' duration, "The patient has been under my care for over a year, and I can see but little improvement in her condition. She thought at one time that pilocarpine did her good."§

The uselessness of a "tonic treatment" has been shown again and again. Dr. Benson|| records a case of eight years' duration in which this treatment was persisted in for five months "without any effects." The thyroid extract was given by the mouth, and in less than a month she became a "new creature."

We must conclude, therefore, that by such treatment little could be hoped for beyond producing a very temporary benefit by improving the appetite and increasing the action of the skin.

\* "Lancet," October 22, 1892.

† "Sheffield Medical Journal," No. 1, October, 1892.

‡ "Lancet," January 21, 1893.

§ "Medical Reprints," September 15, 1892. "Report of Two Cases of Myxœdema with one Autopsy."

|| "Brit. Med. Journ.," April 15, 1893, p. 795.

*The Treatment of Myxœdema by Thyroid Grafting.*

So much for the older methods of treatment. I now pass on to the more modern form, viz., the treatment of myxœdema by means of the thyroid gland.

First, I will deal with the subject in its primary or surgical aspect, viz., thyroid grafting, and afterwards with the modifications and improvements that have since been introduced, by which the treatment has been simplified, rendered more efficient, and at the same time taken out of the hands of the surgeon and given into those of a larger class of men—the physicians and general practitioners.

It was in February, 1890, that Prof. Victor Horsley suggested the transplantation of the thyroid of a healthy sheep into persons affected with myxœdema, with the view to arresting the progress of the disease, basing his arguments on the experiments of Schiff, Eiselsberg, and his own.\* These experiments went to prove that, when the myxœdematous process (cachexia strumipriva) developed in an animal deprived of its thyroid gland, the animal could be kept alive and in good health by the transplantation of the same gland from another healthy animal.

Cases are often recorded in the medical journals immediately after an operation or at the commencement of a new form of treatment, and we hear no more about them. Some of these are exceedingly interesting, and we should like to know how the case progressed and what was the final result of the treatment recommended. A case in point is that of thyroid grafting for myxœdema. Now that the subject of myxœdema is attracting so much attention, it would be interesting to know what has become of those patients who have been treated by this method, whether they show any permanent improvement, and how this mode of treatment compares with that of the subcutaneous injection and ingestion of the thyroid extract in this disease.

With this object I have collected together all the cases of which I know, and, where possible, have obtained further information concerning them. Let us see what have been the results so far.

M. Lannelongue, of Paris,† appears to have been the first

\* "Note on a Possible Means of Arresting the Progress of Myxœdema, Cachexia Strumipriva, and Allied Diseases." "Brit. Med. Journ.," Feb. 8, 1890, p. 287.

† "Lancet," March 22, 1890, p. 665.

to carry out the operation. He reported his case to the Biological Society on March 7th, 1890, immediately after the patient had recovered from the operation and before any change in the patient's condition had occurred. No further information concerning this patient has been reported in the English journals, and we do not know if any improvement followed the operation. On September 3rd, 1890, M. Walther\* performed a similar operation on a woman, 40 years of age, and reported the case to the Medical Society of Paris, the following November: slight improvement with less characteristic appearance of myxœdema was noted. Here again we are left in ignorance as to a later result. In the meantime Drs. Battencourt and Serrano, of Lisbon, reported on the subject of thyroid grafting for myxœdema.† Their case is briefly as follows:—A female, æt. 36, had myxœdema for several years with apparent absence of the thyroid. These observers introduced into the subcutaneous tissue of the inframammary region on each side the half of a thyroid gland of a sheep. An immediate amelioration was produced, which was first marked by an elevation of the temperature. The red blood corpuscles rapidly increased in one month from 2,442,000 to 4,447,000. The patient's movements became more easy, her speech less affected, and perspiration returned. The œdema went down, and her weight diminished from 239 lbs. to 227 $\frac{3}{4}$  lbs. Menstruation now lasted only four days, whereas, previously, it was many weeks. It is to be noted that Battencourt and Serrano state, "The fact that amelioration commenced so soon seems to indicate to us that the thyroid tissue was absorbed."‡ This account, which appears to have been written about a month after the operation, is the latest to hand.

Mr. Hurry Fenwick§ first performed the operation in this country. It was on a woman, and was carried out at the request of Dr. Sansom. No improvement followed, for "the disease was too advanced to admit of any satisfactory inference being drawn as to the efficacy of the method." The case was fatal on the fifth day.

On April 2, 1891, Dr. W. J. Collins transplanted the thyroid gland of a sheep into a patient at the Temperance Hospital at the suggestion of Dr. Ridge.|| The patient was a woman

\* "Lancet," Nov. 29, 1890, p. 1192.

† "La Semaine Médicale," Aug. 13, 1890.

‡ For the translation notes of this case, and from which the above is taken, I am indebted to my friend Dr. Boyce.

§ "Lancet," May 2, 1891, p. 1003; also "Brit. Med. Journ.," Oct. 10, 1891.

|| "The Medical Pioneer," Oct., 1892, and "Lancet," May 2, 1891, p. 1003.

aged 34. The symptoms, which commenced two years back, do not appear to have been advanced. Dr. Collins' latest remark on the case was in September, 1892. He says: "She pronounces herself in good health, is cheerful. Those who watched the patient most closely insist upon mental improvement having taken place, and there are not wanting more material points in which involuntary misconception is less probable."

Of the two remaining cases of thyroid grafting, that of Dr. Thomas Harris and Mr G. A. Wright was reported fully in the "*Lancet*."\* The patient, a woman aged 48, who had shown signs of the disease for nine years, had, on April 4th, 1891, at the Manchester Royal Infirmary, part of the thyroid of a young monkey inserted beneath the breast. The operation was quickly followed by improvement in some respects, but in a few weeks the patient appears to have relapsed completely into her former state. She improved slightly again on returning to the Infirmary, a fact which the authors attribute to hospital diet and surroundings. Her speech remained quite unaffected. In reply to an inquiry as to the condition of the patient more recently, Mr. Wright, on October 18th, 1892, writes as follows: "The myxœdema case has not turned up lately, but when I saw her last she was much the same as before, though she thought herself better. Nothing further has been done so far as I know. My impression was that the stay in hospital improved her a good deal more than the thyroid grafting."

On the 2nd March, 1892, Dr. John Macpherson† showed a patient at a meeting of the Edinburgh Medico-Chirurgical Society on whom he had performed this operation on the 22nd October previously. The patient, who was an inmate of the Stirling District Asylum, was a woman, 39 years of age, with myxœdema of three years' standing. A remarkable mental and physical change followed rapidly on the operation, and appears to have continued for a time. On October 11th, 1892, Dr. Macpherson was good enough to write me: "My patient has quite recently been readmitted into this asylum. When formerly under my care she was melancholic, stuporose, and otherwise manifested the usual mental concomitants of myxœdema. On this occasion she is mildly maniacal, and she presents none of the mental or physical symptoms of myxœdema."

\* "*Lancet*," April 9, 1892, p. 798.

† "*Edin. Med. Journ.*," May, 1892, and "*Lancet*," May 12, 1892, p. 609.

Writing again under date of May 11th, 1893 (just seven months later), he says: "The case is still under my care in this asylum. She is subject to slight recurring attacks of mania and melancholia, the latter, when it occurs, being characterized by mild stupor. Occasionally there appears on her cheeks the characteristic pink flush of myxœdema—the only symptom, if one accepts the mental disturbance as doubtful, of myxœdema. I am quite prepared to observe a relapse in her condition at any time. It suggests to my mind the possibility that there is just sufficient thyroid secretion being produced to prevent pathological symptoms, and that occasionally when the production falls below the necessary requirement of the system the mental symptoms make their appearance."

In this case, in which the myxœdema seems to have been more or less cured, there is raised the question as to the cause of the insanity, and this case would appear to make it the more difficult to explain the reason for the insanity that follows on myxœdema.

In addition to these cases, at a recent meeting of the Clinical Society of London, Dr. Ord said he had tried implantation of the thyroid gland with only temporary success.\*

NOTE.—The operation of thyroid grafting for cretinism is commented on elsewhere. The results of Bircher ("Sammlung klinischen Vorträge," No. 357, 1890) and Kocher, obtained by thyroid grafting on the subjects of cachexia strumaprima, are not here referred to, as they form a slightly different class of cases.

From the above references it will be seen that regarding the ultimate effect of the treatment in the earliest cases, those operated on abroad, we are ignorant, and it is to be hoped that an endeavour will be made to trace them. Excluding Mr. Fenwick's case, there remain four cases of which we know something. Of these, two appear to have been followed by a more or less prolonged period of improvement, the others only very temporary. Of Dr. Macpherson's and Dr. Collins' cases there are points worth noting. In the first the insanity returned within a few months, and concerning the second one can read in Dr. Collins' words that signs of the disease are still present although the disease was never advanced.

On the whole, I think we may conclude, therefore, that at present there appear to be no advantages to be gained by the severer operation of grafting over the minor one of subcu-

\* "Lancet," Feb. 4, 1893, p. 248.

taneous injection, or the simple injection of the thyroid principle; moreover, we cannot at present point to a collection of cases such as we now have with the latter where the treatment has been followed by such uniform results.

*Historical Sketch of Recent Modifications in the Treatment of Myxœdema by Subcutaneous Injection and Ingestion of an Extract, etc., of the Thyroid Gland.*

We now come to the more recent suggestion of Dr. George Murray, a pupil of Prof. Victor Horsley. Dr. Murray being struck with the rapid action that was recorded as following the operation of thyroid grafting concluded that this was due to the absorption of the thyroid juice that was still present in the piece of thyroid tissue at the time of implanting, as the interval was too short for the formation of either fresh secretion or new thyroid tissue. Working on this hypothesis, he prepared an extract of the fresh thyroid gland of a sheep by mincing the gland and extracting the principle with glycerine, and injecting this subcutaneously into a patient the subject of well-marked myxœdema. The result was astonishing, and he communicated it to the profession, as already stated, at Bournemouth, in July, 1891.

On the Continent, about the same time, Brown-Séquard and d'Arsonval are said\* to have suggested, from the experimental results obtained on animals by Vassale and Gley, the probable utility of thyroid juice in myxœdematous persons if injected hypodermically. But they do not appear to have carried it into practical effect. Bouchard,† later, came to similar conclusions from his own experience.

Murray's paper appeared in the "British Medical Journal,"‡ and the treatment there proposed, of the subcutaneous injection of a glycerine extract of the thyroid gland of some animal, has since been carried out in a large number of cases, and the results obtained have been almost invariably as satisfactory and wonderful as those first recorded, in many cases even more so.

Up to the present time (May 18th), so far as I have been able to discover, there have been 100 cases published in which this treatment, or some modification of it, has been tried. About 40 of these were actually treated by the subcutaneous

\* "Lancet," Jan. 21, 1893, p. 124.

† "Brit. Med. Journ." (Epitome), Nov. 12, 1892, and "Arch. Gén. de Méd.," Oct., 1892.

‡ "Note on the Treatment of Myxœdema by Hypodermic Injections of an Extract of the Thyroid Gland of a Sheep." "Brit. Med. Journ.," Oct. 10, 1891.

injection of an extract in all respects similar to that used by Murray.\*

A large number of the cases appeared originally in "The British Medical Journal," and the majority of those elsewhere reported, may be found referred to in that journal.† With the exception of two cases they have all been followed by a remarkable improvement in the condition of the patients. The two exceptions were those referred to by Dr. Michell Clarke, at the meeting of the British Medical Association at Nottingham.‡ No details are given, but it is said that "no change resulted from the injections," a fact exceedingly strange when we consider that every other observer who has carried out this treatment has obtained so marked an alteration in the appearance of the patients when the subject of myxœdema. One, therefore, cannot help thinking that some discrepancy must have occurred in the diagnoses or mode of treatment adopted by Dr. Clarke.

Murray's method was a much simpler one than that of implantation, and the risks of a large operation were done away with; at the same time the immediate results were more satisfactory, and the remote were equally good or better.

The next real advance made in the treatment was that proposed by Dr. Hector Mackenzie.§ On July 27th, 1892, being unable at the time to obtain the extract for injection, he commenced to feed a patient at the Royal Free Hospital on fresh thyroid glands. As an equally good result followed this mode of treatment it was continued, and in less than three months the disease was scarcely recognizable. Dr. Mackenzie claims for this method that it has advantages over the subcutaneous mode in that it is more readily obtainable, can be more easily carried out, and is free from many of the risks and other disadvantages attendant on the injection of the fluid extract. The thyroids in this case were pounded and given in a little brandy. He showed that it was sufficient to let the patient eat the thyroid or swallow an extract made with glycerine.

\* I have been informed that some time back Messrs. Brady and Martin alone were supplying the extract for the use of 100 cases, so there are probably now considerably beyond that number of cases undergoing the treatment.

† The earlier cases have also been tabulated by Dr. Robert A. Lundie on much the same lines as that now presented, and appear with his paper, "The Treatment of Myxœdema," which he read before the Edin. Med. Chir. Soc., and are printed in "The Edin. Med. Journ.," May, 1893.

‡ "Brit. Med. Journ.," August 27th, 1892.

§ "A Case of Myxœdema Treated with Great Benefit by Feeding with Fresh Thyroid Glands," "Brit. Med. Journ.," October 29th, 1892.

At the same time as Dr. Mackenzie reports his case, Dr. E. L. Fox, of Plymouth, reports another case of myxœdema,\* whom he had treated at first by the injection of a glycerine thyroid extract, and afterwards by lightly fried and minced glands taken in currant jelly. This was followed by a similar result. The treatment was begun on June 2nd, 1892.

Professor Howitz, of Copenhagen,† however, had already carried out this principle, for on March 22nd, 1892, he commenced feeding a patient with the thyroid gland of calves, and he made known his results on July 6th. He, too, adopted this method on the principle that it was more accessible in daily practice, and was a safer form of administering the remedy.

At a meeting of the Clinical Society of London on January 27, 1893, Dr. Arthur Davies showed a case ‡ in the treatment of whom he had employed a further difference in detail. This was the administration by the mouth of a powdered extract obtained by extracting the active principle with glycerine and reducing the resulting extract to a powder by heat. It was Dr. Mackenzie who first suggested its preparation, which was carried out by Mr. Edmund White, pharmacist to St. Thomas's Hospital.

These various methods, which differ only in detail, have all been since tried on a number of cases, and they differ little in their result. There is invariably the same remarkable improvement and cure recorded. The extract has been given in a variety of vehicles, such as brandy, beef-tea, water, milk, jelly, with pepper and salt, etc., and the gland has been first subjected to a variable amount of cooking, with the object of rendering it more palatable.

It remains for me to mention one more modification that has been introduced by Vermehren, of Copenhagen.§ He records a case of sporadic cretinism whom he treated with success by the administration of "thyroidin." This substance is obtained by the precipitation with alcohol from a glycerine extract of the finely minced gland, and takes the form of a greyish powder. This substance is, of course, equally applicable to cases of myxœdema, and probably differs little, if at all, from the powder used by Davies.

\* "A Case of Myxœdema Treated by taking Extract of Thyroid by the Mouth." *"Brit. Med. Journ.,"* October 29th, 1892.

† *"Brit. Med. Journ.,"* February 4th, 1893, p. 266, and *"Semaine Méd.,"* 8th Fév., 1893.

‡ *"Brit. Med. Journ."* and *"Lancet,"* Feb. 4, 1893.

§ *"Brit. Med. Journ."* (Epitome), April 15, 1893. (*"Deut. Med. Woch.,"* March 16, 1893).

With all these various minor modifications there still remains the one disappointing fact that as soon as the treatment is discontinued the patient relapses, so that in a few weeks the patient gradually passes back into the condition of myxœdema from which he has only too lately been resuscitated. So long as the drug is in use, whether it be by hypodermic injection or the ingestion of the gland or a preparation therefrom, so long the improvement continues ; but let it be dropped for a time, then without fail do we see only too soon the reappearance of the disease. But it has now been proved that only a small dose is needed to maintain the condition, and that not at very frequent intervals, and the taking of an occasional dose is surely a hardship not hard to bear even were it necessary for the remainder of the patient's life. Although at present there are wanting real indications of a permanent cure, it would seem that after a considerable period the dose may be reduced to a mere trifle, and who knows but that it may finally be dispensed with altogether !\*

*(To be continued.)*

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*General Paralysis Occurring about the Period of Puberty.*

By J. WIGLESWORTH, M.D.Lond., M.R.C.P., Lecturer on Mental Diseases, University College, Liverpool, and Examiner in Mental Diseases, Victoria University.

We are in the habit of regarding general paralysis as in the main a disease of the prime of life—of a time when the fresh vigour of youth has subsided, but before the first touch of decay has laid its hand upon the organism ; when the mental faculties are strained to the utmost in the pursuit of wealth or pleasure, or social distinction, or in the keen struggle for existence entailed upon so many of our race. We are not indeed unaccustomed to meet with cases of this disease occurring both before and after this epoch of life, but the association of general paralysis with the period of childhood and puberty has hitherto been a very unfamiliar idea. Nevertheless, scattered cases have from time to time been published which tend to show that the period of life which appears to offer most exemption from all the ordinary causes of the disease may still claim its victims, and that at, or

\* Such, too, are the views of Dr. Robert Lundie, as contained in an interesting and popular article, "A New Departure in Medical Treatment," which he has lately contributed to "Chambers's Journal," May 6, 1893.

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## PART 1.—ORIGINAL ARTICLES.

*Presidential Address delivered at the Fifty-Second Annual Meeting of the Medico-Psychological Association, held at the Palace Hotel, Buxton, 28th July, 1893, by J. MURRAY LINDSAY, M.D.*

GENTLEMEN,—The difficulties connected with the selection of a suitable subject for the Presidential Address of our Association, which is holding its 52nd annual session, are increasing year by year, for it can readily be imagined that almost every conceivable subject has been well threshed out by my numerous predecessors. After the careful and elaborate work of Dr. Hack Tuke and others there is very little to add to the history of psychological medicine.

The history and work of our Association have also received of late years considerable notice at the hands of previous Presidents. I propose to continue the history up to date, to touch on some points in connection with the organization and work of our Association, to offer some free criticisms on lunacy administration, indicating some alterations and reforms in the lunacy laws and the management of asylums, drawing to some extent upon a somewhat varied and moderately long experience. In this way I hope to rouse some slumbering spirits and to stimulate discussion which I trust may serve some useful purpose.

In 1861 Professor T. Laycock, in his Presidential Address, in speaking of the objects and organization of our Association, referred to its shortcomings and defective organization. But we have moved forward since then, and there can be no doubt that the Medico-Psychological Association, a title adopted in 1866 under the presidency of Dr. W. A. F. Browne, Lunacy Commissioner for Scotland, whose memory I revere and warmly cherish, has progressively advanced in

*The Treatment of Myxædema and Cretinism, being a Review of the Treatment of these Diseases with the Thyroid Gland, with a Table of 100 Published Cases.* By CECIL F. BEADLES, M.R.C.S., L.R.C.P., Assistant Medical Officer, Colney Hatch Asylum.

(Concluded from p. 355.)

### *A Criticism of Published Cases.*

(See Tables 1a and 1b.)

For the benefit of those who have not followed the recent discussions I have compiled tables of the cases of myxædema treated by thyroid injection and feeding that have thus far been published in this country. These, I trust, will be found useful and easy of reference. The main points of each case are arranged under a few convenient headings, viz., the sex and age of the patient, the duration of the disease, the length of time the treatment had been carried out at the time of reporting, the dosage and method of administration employed, the results obtained, and, where such existed, any ill effects that were seen to follow or occur during the course of the treatment. In all there are details of 100 cases shown. A glance at this summary will bring out certain points of interest and importance.

1. The female sex largely predominates, there being only eight male cases, but then it is to be remembered that the disease is far more common in women than in men; the Clinical Society's Report gives the proportion as one to six, but this is undoubtedly too high. The table shows, however, that we may look for equally favourable results in both sexes.

2. There is no limitation of age; the thyroid gland appears to exert the same remarkable influence alike on the young, middle-aged, and those past the prime of life. With regard to the very young I shall have occasion to speak shortly when dealing with the subject of cretinism, and I shall return to the subject of the administration in elderly persons.

3. The length of time during which the disease had existed is seen to make little or no difference. For instance,

in Dr. Corkhill's case\* the patient is said to have only exhibited signs of the disease five months, whereas in one of the cases reported by Dr. Dunlop† it was of twenty years' duration; between these extremes all stages exist. This is contrary to what might have been expected, and, certainly, at first sight, one would scarcely have hoped to obtain the same marked results where the disease has been a long time in existence. It is, however, in the extremely marked cases that the change is most pronounced, and, on the other hand, the cases in the very earliest stage of the disease seem less noticeably influenced even after a prolonged course of treatment. This point was brought out in the cases published by Dr. G. E. Hale,‡ who wrote me last October: "In three, considerable improvement occurred after periods of seven or eight weeks, all three being able after the course to do a good day's work. In the fourth case, an early case in a young woman, little or no improvement has occurred, although the treatment has been perseveringly followed out for more than six months."

The same applies to two early cases on whom the treatment has been tried in Colney Hatch. They improved slightly after a time, but there was not the rapid change so uniformly noted in advanced cases as being at once observable.

4. The period during which the treatment has been carried out at the time of publication has varied considerably in different cases, from a few weeks to many months, but in all there is the same result recorded. Dr. Murray's is the longest, it is now over two full years, he having begun treatment in April, 1891.§ A most singular point is the rapidity with which a change in the patient's condition is first recognizable, and even a cure may be said to have taken place. The treatment owes its origin to the change that was recorded as occurring within a few hours of the transplantation of the thyroid. The patient under my care seemed brighter within twenty-four hours of the first injection. In Dr. Napier's patient|| a change for the better was first noticed after the fourth injection, and the patient

\* "Brit. Med. Journ.," Jan. 7, 1893.

† "Edin. Med. Journ.," May, 1893, p. 1012.

‡ "Brit. Med. Journ.," Dec. 31, 1892.

§ "Lancet," May 13, 1893, p. 1131.

|| "Notes of a Case of Myxædema Treated by means of Subcutaneous Injection of an Extract of Sheep's Thyroid," with photographs. "Glasgow Medical Journal," Sept., 1892.

was discharged in two months, after sixteen injections of one gramme of a watery extract of the thyroid, with disappearance of all the characteristic signs of the disease. Again, in M. Bouchard's two patients the improvement is said to have been "extraordinarily rapid."\* Dr. Mackenzie's first patient "had very considerably altered for the better"† at the end of a fortnight's feeding with thyroid glands, and Mr. Shapland's case expressed herself as "feeling better than she had done for years" after taking half an underdone gland every morning for a week.‡ Two days after the first injection of mxxx. of fluid extract a patient whose photograph and case is published by Dr. Henry, of Lewisham,§ showed distinct signs of improvement. The changes brought about in one month to eight weeks are always well marked. Again, with two of the more recently exhibited cases, viz., Drs. Wood's and Johnson's, "distinct improvement was discernible on the third day."|| The length of time during which it may be necessary to continue the treatment is a point as yet unknown. The probabilities, however, are that it may be necessary to continually give a small dose at more or less prolonged intervals in order to maintain the improved state which has been brought about.

5. As to dosage there has been no uniformity, and almost every observer has given according as he thought best. This want of uniformity is, of course, due to the fact that we are still (so to speak) in the experimental stage of the drug, and it has not been found possible as yet to fix the correct dose—that is to say, an amount of the extract which is capable of producing a curative effect without at the same time giving rise to toxic symptoms. The quantity and frequency of administration, however, are points that will probably be shortly decided. At the same time, they will probably depend on the stage of the disease and the age of the individual; moreover, they may possibly vary with individual cases and the idiosyncrasies of the patient. With these varying factors special care will be needed in its employment.

Another point that cannot be decided as yet is the best mode of administering the thyroid gland, or, rather, its

\* "Lancet," Oct. 1, 1892.

† "Lancet," Jan. 21, 1893.

‡ "Brit. Med. Journ.," April 8, 1893.

§ *Idem.*

|| "Brit. Med. Journ.," May 6, 1893, pp. 954 and 955.

active principles. As is shown in the list of published cases, various minor modifications of the original method have been adopted. These, which already have been referred to, have each been lauded as the best by those who first introduced them, and it is only from the experience of others and their more extensive trial that we can arrive at a correct estimation of their proper value. There is no doubt that some of these methods have advantages over others, and that with some there are distinct objections to their use as being more liable to be followed by ill-effects. At the same time, it may be that what is preferable in one case may not be so in another. To this subject I shall return.

6. But what is clear from all the cases that are here collected together is that this special mode of treatment is invariably followed by an improvement in the patient's bodily condition, by a rapid change in the appearance of the patient, and within a remarkably short space of time (measured by a few weeks) the patient has so far recovered from the disease that it is impossible in many cases to recognize the case as one of myxædema. The general puffy, œdematous-like swelling disappears, and the coarse, dry skin is replaced by one that is smooth, soft and moist, and the blunted, thickened features so characteristic of myxædema are rapidly lost; the hands become smaller; within a comparatively short space of time young hair commences to grow on the scalp and eyebrows, so that in place of the thin, scanty crisp hair the head is soon covered by a thick healthy crop of hair, which causes a most noticeable alteration in the appearance of the patient. The body-weight rapidly diminishes, often as much as a stone a month, until it has reached a certain point, when it again tends to slightly rise. This loss of weight is probably due to the absorption or conversion of the mucin in the tissues, and the increase which afterwards occurs may be due to a deposit of healthy fat in its place. The special senses all become more acute, eyesight and hearing improve, and general tactile sensation becomes more natural; the bodily functions assume their normal action, the bowels and catamenia become regular, and there is often an increase of urine passed; the voice loses its peculiar slow, thick, monotonous form, and assumes its original type. The patient becomes warmer and feels more comfortable, and there is a rise of the body temperature, which nearly or

quite reaches the normal point. Both mind and body become more active. The patient becomes brighter and more cheerful, and is able to get about and attend to his duties, in which he now takes an interest. This, in short, is only another way of saying that there is a complete transformation, and that the patient has ceased to be a patient, and appears a new individual. Such, briefly, are the results that have been attained.

7. But this startling result has not always been obtained without the occurrence of some grave and unpleasant symptoms. These have doubtless been due in the majority of the cases to an excessive dose of the preparation, manifesting a toxic action, and are capable of, and to a great extent have been overcome by more careful regulation of the dose.

As a rule, when occurring they have been of a mild nature, such as general weakness, faintness, nausea, vomiting, slight giddiness, headache, and aching pains in the neck and shoulders, which have rapidly passed off on reducing the dose, but occasionally the symptoms have assumed a more serious nature, and, at least in four instances, death resulted. This happened in the early days, of the thyroid treatment, and such a result it is to be hoped will not again occur. Amongst the more severe forms of symptoms to be guarded against are loss of consciousness, tonic spasms, collapse, urgent dyspnoea, and cardiac failure. These have been prevented by greater care in regulating the amount and allowing it to be administered more slowly. With a more accurate knowledge of the power and action of the new remedy they are lessened or altogether avoided. The liability to irritation, erysipelas, abscess and induration sometimes following subcutaneous injections has been lessened by greater antiseptic care, and by the more recent administration of the extract by the mouth has been entirely prevented.

As the discomforts and risks of the treatment have been so fully gone into by other writers, notably by Dr. Lundie\* and Prof. Grainger Stewart,† I will abstain from further entering on the subject. The latter observer gives some useful advice for the treatment of urgent symptoms that may arise.

But still, I may remark, it is clear that in the active

\* "Edin. Med. Journ.," May, 1893.

† "The Practitioner," July, 1893.

principle contained in the thyroid gland we have an exceedingly powerful chemical body, and too much care cannot be exercised in its proper use. In persons suffering from very advanced disease, and in elderly subjects, great caution is necessary, and with returning strength and vigour moderation in all forms of exercise should be insisted upon.\*

*The Treatment, with Special Reference to the "Insanity of Myxœdema."*

The actual number of recorded cases of myxœdema in which definite insanity ensued in the course of the disease is comparatively few,† and only one or two have been published by medical officers of our asylums. But if we remember the mental state which patients who are the unfortunate subjects of myxœdema invariably develop as the disease becomes advanced, we can understand how a considerable number of them eventually find their way into lunatic asylums. It is probable that these institutions are the last home of a large percentage of cases, and there are probably few asylums of any size where such patients do not exist, and, owing to the chronicity of the disease, are probably resident for a long period.

Myxœdematous patients invariably become demented. Dr. Savage, in his review of the Clinical Society's Report on myxœdema in Dr. Tuke's recently published admirable "Dictionary of Psychological Medicine," says:—"In a rather large proportion there is more or less imperfection of

\* It would seem impossible that the condition described by Dr. James Whitwell ("Brit. Med. Journ.," Feb. 27, 1892), as found by him in the cortical cells of the brain in a case of myxœdema, can be present except in perhaps the rarest instances, even in the most advanced cases of the disease. Otherwise, how is it possible for the cells to recover to the extent which one would judge must occur with the change in the patients brought about by the thyroid treatment? In like manner it is not easy to explain how the vessels of the brain could recover from such advanced endarteritis and periarteritis as was found to be present in a case of myxœdema by Dr. Rubert Boyce and myself ("Journ. Path. Bact.," No. 2, Oct., 1892). It is clear there is much yet to learn of the pathology and cause of the disease. That such a diseased state of the vessels sometimes exists proves that great care should be exercised in the use of the thyroid juice.

† The following may be referred to:—Clonston, "Clinical Lectures on Mental Diseases," 1883, p. 603. Blandford, "Insanity and its Treatment," 1884, p. 86. Savage, "Journ. Ment. Sc.," Jan., 1880, p. 417. J. C. Mackenzie, "Journ. Ment. Sc.," July, 1889. Ernest White, "Lancet," i., 84, 974. Urquhart, "Lancet," i., 84, 1079. Jürgens, "Lancet," i., 90, 484. Cecil F. Beadles, "Journ. Path. and Bact.," No. 2, 1892. John Macpherson, "Edin. Med. Journ.," May, 1892. James Whitwell, "Brit. Med. Journ.," i., 92, 430.

mental processes, the defect being one of retardation or sluggishness." The development of actual insanity with delusions, sometimes with attacks of excitement, is not uncommon. "Delusions and hallucinations occur in nearly half the cases, mainly where the disease is advanced. Insanity as a complication is noted in about the same proportions. It takes the form of acute or chronic mania, dementia, or melancholia, with a marked predominance of suspicion and self-accusation; exalted ideas may occur. Memory is usually impaired from an early period. It is recorded as deficient in forty-six out of seventy-one cases."\*

The authors of many of our text-books on insanity make no reference to myxœdema in its relation to brain disease, and the remainder pass it over in a few words. Dr. Clouston, however, refers to three cases that were under his care at the Royal Edinburgh Asylum for the Insane, "who were positively insane," and adds, "all the examples of the disease I have ever seen were more or less affected mentally, if they were not technically insane."†

No work on insanity to which I have referred speaks of any special treatment for these cases; this is undoubtedly due to the only recently thoroughly recognized, and even then considered incurable disease, and is a feature which will probably receive attention in future editions.

I have already spoken of and commented on a case in which thyroid grafting was adopted with a partial amount of success (see *ante*, page 350).

There are now several recorded cases of myxœdema with insanity that have been treated by the subcutaneous injection of the thyroid juice or by feeding.‡ Dr. Ernest Carter, of Whittingham Asylum, was one of the first to report upon the treatment.§ His case was that of a female lunatic aged 43, with myxœdema of over four years' duration, and whose insanity had existed five years. After a three months' course of injections the patient's bodily condition was much improved, but, at the time of writing, complete recovery of her mental power had not taken place. In Dr. Claye

\* Tuke's "Dictionary," Vol. ii, p. 828; art., "Myxœdema and Insanity."

† "Clinical Lectures on Mental Diseases," Clouston, 1883, p. 603. In a note in the "Edin. Med. Journ." of May, p. 1057, Dr. Clouston makes mention of eight cases which have been admitted into the asylum.

‡ At Newcastle Dr. Clouston reported two cases of insanity in which improvement was manifest from thyroid feeding; one cured in four months, the other in six.—"Brit. Med. Journ.," Aug. 26th, 1893.

§ "Brit. Med. Journ.," April 16, 1892.

Shaw's case,\* however, the patient was discharged from Banstead Asylum, recovered, after a treatment of two months. This also was a female who had showed myxœdematous signs four years, and been the subject of recurrent melancholia for a period of ten years. The case that was under my care at Colney Hatch Asylum, and of which I have elsewhere published the early notes,† had greatly improved in little over a month, if we count from the time the injections were commenced regularly. The change in her mental condition was even more pronounced than that in her bodily, and was one that I never thought it possible to attain.

Dr. Melville Dunlop, of Edinburgh, has published a series of six cases of myxœdema treated by thyroid feeding.‡ One of these (Case II.) was undoubtedly insane at the time. It is a particularly interesting case, and I make no excuse for referring more fully to it.

The case was one of a lady who had shown signs of myxœdema over 12 years, and in whose family there were others affected in the same way, viz., her mother and a twin sister. She had been a complete invalid, and unable to move either her hands or legs for something like eight years. Memory had become defective and she wandered in her talk. A few months before treatment was commenced she became much worse, especially mentally, becoming childish, with hallucinations of sight, smell, and hearing, sleepless, restless, and refused food. At length acute mania supervened, when she was excited and dangerous, and for six weeks had to be under the care of special mental nurses. On October 18th, while in this state, the thyroid feeding was begun. xxx. of thyroid extract were administered thrice weekly. "By the 30th of October the excitement had quite gone, and the patient was resting and sleeping quietly. She had no longer any hallucinations, and was speaking rationally." By November 12th there was some improvement in her bodily condition, and the extract was reduced to twice a week. A month later there was a marked change. In January the extract was given only every alternate week. She continued to improve mentally and bodily, and in the early part of February (a four months' course) many of her friends could scarcely recognize her.

Dr. Hamilton C. Marr, of Woodilee Asylum, also reports a case treated by feeding.§

\* "Brit. Med. Journ.," Aug. 27, 1892 (communicated by Dr. Stansfield to the annual meeting of the B.M.A. at Nottingham).

† "Brit. Med. Journ.," Dec. 24, 1892.

‡ "Edin. Med. Journ.," May, 1893.

§ "Glasgow Med. Journ.," Aug., 1893.

This is a woman aged 51, whose mental aberration dated from Christmas, 1887, but whose bodily weakness commenced three years previously. She was incoherent and subject to attacks of excitement and violence, at which times she would make false accusations against her attendants. During the intervals she was melancholic and refused to speak. Her health had become very feeble and she had taken to bed. Treatment was commenced in February, 1893, by giving a quarter of a sheep's thyroid mixed with bread crumbs and sherry. After three weeks this was replaced by a glycerine extract, two ounces of which represented one whole gland; of this one drachm was given thrice daily. "The patient gradually improved under treatment," and now it is said that she can converse quite intelligently and is very cheerful in disposition, giving a helping hand to the nurse. Hearing has improved and the swelling of the body has gone down.

Quite recently I have heard of another case of myxœdema with insanity that has undergone the treatment. It is the case which Dr. J. F. Woods, of Hoxton House Asylum,\* showed at the Hunterian Society on April 12th.

A female, 32 years of age, with myxœdema of 15 months' duration, of whom it was said that she "began to improve on the third day." Concerning this patient, Dr. S. Whitaker kindly informed me, on August 3rd, that, before treatment was commenced, she had physically most of the signs of myxœdema and "mentally her speech and mental processes were slow, she often heard voices and saw spirits, she was very obstinate, and used to stand or sit about all day and never employed herself. Her weight was 9st. 6½lbs. at the commencement of treatment on January 20th. The treatment was discontinued on June 8th, when her weight was 8st. 6lbs., she had lost most of the physical signs of myxœdema, and mentally she was bright and talkative and employed herself, but she still occasionally heard voices and saw spirits, though not so much as formerly. Since June 8th there has been no apparent change, and to-day (August 3rd) her weight is 8st. 8lbs."

As regards the special mode of administration employed, Dr. Whitaker says that at first the medicine was given twice a week as hypodermic injections of the thyroid extract, but afterwards, and "with better effect," she took White's powders by the mouth. After the first three months the powder was only given occasionally, and during the latter part of the time, in place of the powder, a "thyroid mixture" in ʒss. doses,† each ʒss. being equal to ¼th of a gland, and that this seemed to agree with her the best.

\* "Brit. Med. Journ.," May 6, 1893.

† The extract for hypodermic injection was obtained from Brady and Martin, and the "thyroid mixture" prepared by Mr. Chas. Allen.

It is now proposed to let the patient have a dose about once a month.

Under this heading I may perhaps as well call more pointed attention to the change following upon the treatment that has taken place in the mental condition of those patients who have not been regarded as insane, but who have shown the more or less marked dementia that is characteristic of advanced myxædema. Thought, like speech and actions, is slow, and memory is impaired or lost, and sometimes there are distinct delusions of a suspicious nature, which yet are not sufficient to have the patient certified as a lunatic.

In all these cases, as I have already said, the patient becomes brighter and the mind more active; memory returns and delusions have frequently been lost. Some of these cases will be found referred to elsewhere in the present paper. Drs. Murray, Mackenzie, Davies, Maude, and others all bear testimony to the unquestionable mental improvement that invariably occurs, and as Dr. Hingston Fox says of his patient, "not only has the physical condition altered, but mentally the change is also great. She feels much lighter, less burdened, as she says, and the depression of spirits has largely passed away."\* In a note I received on May 18th Dr. Davies tells me that in one of his cases the mental activity for carrying out arithmetical calculations was greatly increased by the treatment, and in others the hearing has been very markedly improved.

Seeing what has thus been done in this line, it appears to me only right that an attempt should be made in these cases to allow the patient the benefit of a trial of one or other of the methods employed in the treatment, and in our asylums should certainly be carried out as a treatment for the insanity of myxædema.

Although I do not intend to enter on the pathology of myxædema in the present paper, one cannot help remarking that we can see, in the results that have recently been obtained, strong evidence in favour of the view that the insanity of these cases is dependent primarily, if not entirely, on the disease or atrophy of the thyroid gland and not on a primary change in the brain.†

\* "Trans. Hunterian Soc.," 1892-3.

† I would suggest that in those few cases where insanity antecedes the appearances of myxædema, the presence of the two diseases is a mere coincidence.

*The Thyroid Gland in the Treatment of Cretinism.**(See Table II.)*

Just a word or two on the subject of congenital myxœdema, or sporadic cretinism, as it is more commonly called in this country. Fortunately such cases are of less frequency than myxœdema in the adult. Of the number in this country I have no idea, but there are probably some in all our imbecile asylums. I have seen two quite recently at Leavesden. They were both males, and showed the disease in its characteristic form. Children born in that condition have been thought hopelessly imbecile, and quite incurable. They have lived a wretched, automatic existence for a variable length of time, rarely reaching beyond 30 years of age, as a rule being ultimately carried off in the winter months. No treatment beyond attempting to keep them warm by clothing and surroundings has hitherto been considered of use.

Victor Horsley, who contributes an interesting article on cretinism in the "Dictionary of Psychological Medicine," says: "A good deal can be done in the direction of palliation" by keeping the patient very warm in a hot atmosphere, thoroughly clothed, the employment of hot air and Turkish baths, and the internal administration of pilocarpine or tincture of jaborandi.

Now we can look for a better result. Horsley, writing on the same subject, remarks: "No treatment of cretinism has ever been attempted from the point of view suggested by the pathology, for the reason that until recently the latter has been so extremely obscure. It is obvious, however, that where the idiotic condition can be shown to be originated by loss of function of the thyroid body, an attempt should be made to restore that function. The only way in which this would be possible would be by the method originally suggested by Prof. Schiff, viz., transplantation of the thyroid gland."\*

Cases have lately been published in which the thyroid treatment has been carried out with a marked change in the condition of the patient.

Dr. John Gibson, of Brisbane, records the following case:—

Male cretin, aged seven years, on whom he had twice grafted the thyroid gland from a lamb, first into the right mammary region on July 20, 1891, and again on May 20, 1892, he introduced

\* "Dictionary of Psychological Medicine," Hack Tuke, 1892.

a gland into the peritoneal cavity. The paper which he originally read before the Intercolonial Medical Congress of Australia last year was published in this country last January.\* The numerous accompanying illustrations, reproduced from photographs, show a marked change in the appearance of the child, a brighter and more intellectual look is especially noticeable. He had grown two inches. Four months after the second grafting Gibson concludes his remarks by, "To all appearance he is now merely a well nourished baby boy, with soft, natural skin, and firm limbs, with somewhat thick features and lips, but no myxœdematous swelling. The grafting, to sum up shortly, has cured his myxœdema, and has lessened his cretinism."

Only a few months ago the following case was published by Dr. Edward Carmichael, of Edinburgh†:—

Cretin about nine years of age. Patient was treated with the hypodermic injection of thyroid extract. Commencing in April, 1892, the injections were continued until October, when feeding with the raw gland was substituted. The accompanying photographs show a marvellous effect, and the observer states that "The result of the thyroid treatment was continuous improvement. As week by week passed some mark of improvement was always seen. Marked improvement in intelligence was seen in many little actions." The patient could not be recognized by friends as the same child.

These two cases show what may be expected, no matter which mode of introducing the thyroid is preferred. In addition to these, Dr. Affleck‡ showed at Edinburgh "a case of sporadic cretinism in a young man which had been greatly improved by implantation of thyroid on three occasions." Dr. John Thomson§ has treated a couple of cretins, aged respectively four and 18 years, by feeding, with "wonderful success." Dr. Byrom Bramwell showed a girl aged  $8\frac{1}{2}$  years at the Edin. Med. Chir. Soc., on February 16, whose "mental condition had become completely transformed," and who had grown an inch in height after five weeks of thyroid feeding.|| It was on a case of adult female

\* "The Function of the Thyroid Gland, with Observations on a Case of Thyroid Grafting," "Brit. Med. Journ.," Jan. 14, 1893.

† "Cretinism Treated by the Hypodermic Injection of Thyroid Extract and by Feeding," "Lancet," March 18th, 1893.

‡ "Brit. Med. Journ.," Feb. 25, 1893, p. 411, and "Edin. Med. Journ.," May.

§ "Brit. Med. Journ." and "Lancet," Feb. 25, 1893, and "Edin. Med. Journ.," May. The latter case is reported in full on p. 1022, and is accompanied by illustrations.

|| "Edin. Med. Journ.," May, 1893, p. 992.

cretin that Vermehren, of Copenhagen,\* used, with success, the preparation which he has called "Thyroidin," and he has since used it with like result on another. Dr. A. G. Francis, of Hull, has informed me of a case of congenital myxœdema, as much as 36 years of age, whom he has under his care, and who "is improving immensely" under thyroid treatment.†

There is one more case recorded in which the thyroid has been employed in the treatment of cretinism. This was the case of Dr. V. Robin, of Lyons.‡ The fresh juice from sheep's thyroids was injected daily into a child of seven years of age. "Improvement was immediate. In fact the child is quite unrecognizable to those who knew it before treatment." The injections were afterwards supplemented by successfully grafting two lobes of a sheep's thyroid in the submammary region.

Dr. William Robinson, of Darlington, has not been so successful. He informs me that the case of sporadic cretin that he referred to in the "*Brit. Med. Journ.*"§ as being slightly improved by thyroid extract was a female aged 10½ years, who had weekly injections of an extract prepared in accordance with Dr. G. Murray's directions. The dose was given beginning with six and increasing up to thirty minims for two months, after which one thyroid gland was eaten weekly for several weeks. The result was only very slight improvement—"not sufficient to justify further treatment." In a second case, a male semi-cretin, aged 28 years, there was "no visible improvement" after a similar two months' course of hypodermic injections.

Although the result here was disappointing, and also in a male cretin, aged eight, who was referred to by Mr. Evans at a meeting of a medical society on March 24th, "who for six weeks had taken one thyroid lobe twice a week without any improvement,"|| such a result appears to be rather the exception than the rule, and we may expect to see great benefit derived from the new treatment in this supposed incurable disease. It is possible that by applying the remedy after the manner of Robin the best results are to be obtained.

\* "*Brit. Med. Journ.*" (Epitome), April 15, 1893, and "*Deut. Med. Woch.*," March 16, 1893.

† "*Brit. Med. Journ.*," April 8, 1893, and Private Letter dated Aug. 5th.

‡ "*Brit. Med. Journ.*" (Epitome), Sept. 10, 1892, and "*Lyon. Méd.*," Aug. 7, 1892.

§ "*Brit. Med. Journ.*," Jan. 7, 1893, p. 38.

|| "*Brit. Med. Journ.*," April 8, 1893, p. 767.

*Personal Experience of the Treatment in Myxædema with Insanity.*

It has been my good fortune to see four cases of myxædema treated by this modern method in Colney Hatch Asylum during the past twelve months, and so I have been able to notice closely what changes and improvement actually took place in the patient's condition, both bodily and mentally.

Of the four cases in Colney Hatch, one is that of a woman in an advanced stage of myxædema, whom I myself treated, and whose case I reported in the "British Medical Journal" for December 24, 1892, two were women in an early stage of the disease, and the remaining case is that of a man presenting all the well-marked characters of fully-developed myxædema.

I. First let me refer again to my case of M. B. She was a woman of 50 years of age, with myxædema of at least eight years' existence, and whose insanity, which took the form of religious melancholia, was of  $4\frac{1}{2}$  years' duration. After treatment by subcutaneous injections of thyroid extract, extending over three months, there was great change in her bodily appearance, but the improvement in her mental condition was even more marked. She was cheerful, bright, usefully employed, free from all delusions, and might be considered quite sane; if there had been friends anxious to take her out of the asylum there is no reason why they should not have done so.

After October 4th the injections were discontinued, and unfortunately nothing was done to maintain the improved condition brought about. In a short time the patient slowly but steadily relapsed—that is to say, there was some return to the myxædematous appearance that she previously possessed; her voice became somewhat thicker, hearing less acute, puffiness of face more marked, slower in movements, and she did not feel in such good health, and with this a drop of the temperature again, nearly to its original low position. But she never reached anything like the stage present before the injections were commenced. It is satisfactory to note that her mind was still clear, and has remained so all along.

On February 28th the treatment was renewed in another form. On that day Dr. Seward gave the patient a thyroid powder, representing  $\frac{1}{6}$  of an entire thyroid gland of a sheep.\* Between then and May 9th the patient took 17 similar powders. She then had her photograph taken, which is reproduced as Fig. 2, and for contrast to show the striking change that has taken place in the

\* Supplied under the direction of Mr. Edmund White by C. B. Allen, Pharmaceutical Chemist, Kilburn.



*Fig. 1. M.B. Before commencing treatment.*



*Fig. 2. M.B. A year later, after treatment.*

CASE OF MYXŒDEMA.



patient's condition Fig. 1 is reproduced from a photograph that was taken of the patient before any treatment was commenced, exactly 12 months previously. It may be mentioned that at that time the patient was quite unable to open her eyes owing to the swollen state of her eyelids, and her mind was such that she did not know what was being done, and she has since had no recollection of the event. Her earlier days in the asylum are a perfect blank, from which she was first awakened by the thyroid injections, only, however, to recall events that took place before her admission. In the last photograph taken she has much the same appearance as she had when the hypodermic injections were first discontinued, an appearance which she still maintains.

The patient has now (Aug. 5) had the powders on 33 occasions first at intervals of two or three days, then every fourth day, and now for the last six weeks not oftener than every fifth day. This is found to keep the temperature as nearly as possible at normal; in fact, during the past week there has been a tendency to rise above it. The last three months she has had three grains of a powder obtained from another firm of druggists,\* which has answered equally well. She has always taken the powder in jam after breakfast, and on those days remains in bed until mid-day.

The patient's improved condition is maintained, and she now shows only a very slight degree of the myxœdematous facies, but she is somewhat crippled owing to the old rheumatoid arthritis from which she suffered before the myxœdematous process started; she is, however, able to get about and make herself useful in the ward. She is quite sensible in her speech, and is very cheerful, and she regards her present condition as a happy release from her former wretched state.

Mentally she would be described only as somewhat weak-minded.

The action of the drug upon her joints is remarkable. She suffers intense pain in all her joints after the powders are taken, although recently, perhaps, to rather a less degree. This comes on shortly after the powder is swallowed, and continues for the greater part of the day. This has not been noted in any previously recorded case, and is probably due to the chronic rheumatoid affection of her joints, which remain permanently enlarged and deformed.

The patient's weight, which, after a month's regular injections, fell from 9st. 12lbs. to 8st. 8lbs. (August, 1892), has since gradually increased, and on May 18th had reached 10st. 8lb., notwithstanding the absence of much of the œdema. This has been maintained.

From charts, with a complete record of the patient's tempera-

\* Prepared by Ferris and Co., of Bristol, who with a number of other firms now supply several preparations of the thyroid.

ture since she first went under the thyroid treatment (May 10th, 1892), it is seen that the original subnormal temperature gradually rose and remained about normal so long as the injections were continued, and for a few weeks beyond, after which it again fell to its previous low position, to again ascend when the powders were administered. On a separate chart there was recorded the rise of temperature that followed in the course of the day after the powder was given, the temperature being taken every two hours. It is interesting to note that (as in the case with injections), after the early administrations, there is a very sudden rise and fall again of the temperature, which after a time becomes much less as the normal is maintained, and recently it has only risen a few points during the day.

The two early cases of myxœdema were treated in different ways.

II.—The first is that of L. B., a female, aged 51, who was admitted into Colney Hatch, April 8th, 1892, for melancholia. She was irritable, restless, and quarrelsome, with delusions of suspicion. She had attempted to commit suicide. She was a Jewess and had been married. She presented the signs of the disease in an early stage; there was slight puffiness of her face, the skin somewhat thickened, dry and rough, and her hands large and swollen. Hair scanty and rough. Her voice was inclined to be thick, slow and monotonous, and she was somewhat deaf. Her temperature was sub-normal, never reaching the normal line. Weight, 9st. 11lbs.

While this patient was under my care I treated her by the hypodermic injection of the fluid extract, obtained, as in the case of the other, from Brady and Martin, of Newcastle. Between the 29th August and 4th October she was given 14 injections of *mxx.* each, there being an interval of a day between each, with a few exceptions. She objected strongly to the injections, not because they hurt, but because, she said, that she was "marked for life, and would be turned out into the streets as a thief." At the end of this time there was an undoubted slight degree of change noticeable, although she could not be said to have recovered her senses. Her body temperature rose to a more normal position, and her mental faculties were much clearer. It is possible that further improvement might have followed if the treatment had only been persisted in, but unfortunately it was allowed to drop, and what little improvement had been produced has more or less disappeared, and she is now in nearly the same condition as she was in last August.

III.—The other female patient, M. S., was treated by my colleague, Mr. H. G. Shaw, by the ingestion of raw thyroids. She had been resident in the asylum since December, 1890. She was a

single woman, 45 years of age. She was restless, complained of noises in her head, and had aural hallucinations and optical delusions, and others of suspicion. It had been noticed that her features had been gradually assuming a rather more thickened aspect, and her voice was thicker and more monotonous in character than on admission. She was becoming more languid and slower in her movements, and she suffered much from cold, always being worse when the day was chilly. Her temperature was found to be seldom much above 97°.

It was decided, therefore, to try the effect of the raw gland on her. Commencing in October last, she continued to have them at intervals of one and then two days, for a period of six weeks, on eight different occasions. She took them minced in the form of sandwiches. After the first once or twice she complained of headache and giddiness, but after the later three administrations the ill-effects assumed a more grave form; she had violent pain in the abdomen, followed by loss of consciousness. The administration was, therefore, stopped. For a fortnight the patient remained in bed in a somewhat critical condition, and as during this short course of treatment she lost considerably over two stone in weight, there cannot be the slightest doubt but that the drug was too rapidly pushed, and that better effects might have been expected from a smaller dose. But it is by such experiences that we learn. On November 21st, 1892, it is noted that "a considerable improvement, both mentally and physically, has followed." This patient is now in very good health, but still shows some signs of the myxœdema, although to less degree than last October. She says herself that she is certainly feeling better than she did at that time; she has also been gaining in weight, and in May a luxuriant crop of new hair sprung up on her head. Her mind is clear, she is useful in the ward, and is always willing to oblige.

IV.—I now come to the case of the man suffering from advanced myxœdema, who is now under the care of Mr. F. Bryan, and who will publish the case in full. The patient, J. T., is 33 years of age, and has been an inmate of the asylum six years, being admitted for melancholia, with aural hallucinations and suicidal attempt. In the original certificate it is stated that this condition seems to have arisen from concussion of the brain, the result of accident. From the note made on admission it is evident that myxœdema was present, but not recognized, and it is said that his condition was "suggestive of chronic kidney disease." From further notes it is clear that the myxœdema became more marked, and still remained unsuspected until September 1892, when it was proposed to let him undergo a course of treatment by the thyroid method (injections), but some difficulty arose in having the patient photographed before commencing the treatment, and it was consequently postponed for a time. Meantime the administration of a powder had been proposed, and proved to be followed by as marked

results as that following the injection method, and so it was decided to carry out this mode of administration on the patient.

Treatment was commenced on February 25th of this year, and is being continued at the present time. During the three months that had elapsed, up to May 6th, the patient had taken 23 powders (White's) similar to those used in the case of M. B.; for the first three weeks he had a powder every other day, afterwards one every fourth day. From May 8th to May 23rd half a powder every other day was taken. On May 25th it was altered to five grains (Ferris) every other day, which was continued until June 18th, when the temperature rose to  $101^{\circ}$ , and there was severe vomiting. For three days the patient felt very ill, and his temperature remained high; it then fell to  $96.4^{\circ}$ . Similar powders were commenced again on June 26th, and he had one a week, which has lately been increased to two. Up to the present time (August 5th) he has had the drug on 52 occasions, when he has remained in bed during the morning.

At the time of commencing the treatment the patient had the appearance of a typical case of fully-developed myxœdema, so that there is no need to repeat a minute description of his appearance. By May he had altered to a wonderful extent; he was more healthy-looking, and had lost the characteristic look almost entirely. His hair had grown so that it was quite thick; his voice was clearer, his eyesight improved, and he did not have sudden attacks of blindness, of which he formerly complained. The patient said himself that he was feeling much stronger and better in health, warmer and more comfortable. He had now lost the weakness of which he complained at first after taking the powders.

This condition is being fully maintained. The man is sensible, and appears to be almost if not quite free from delusions. He says that six years ago he was taken to the Middlesex Hospital owing to an accident that befell him, and he remembers being spoken of at that time as a case of myxœdema.

The patient's weight gradually fell from 10st. 12lbs. on February 25th to 9st. 7lbs. on April 29th. Since that date it has been rising, and has now reached 10st. 3lbs. Before treatment his temperature was almost invariably below the 97 line; after the commencement of the treatment it rose to the 98 line, and for some time remained between  $98^{\circ}$  and  $98.4^{\circ}$ , but now it varies between  $97^{\circ}$  and  $98^{\circ}$ . It is also interesting to note a distinct increase in the urine passed during the 24 hours; the amount has gradually risen from about 50ozs. in February to 70ozs. in August.

Beyond the first weakness and the attack of vomiting, with rise of temperature that once occurred, the patient has been quite free from ill-effects.

*Other Cases of Myxœdema treated with Thyroid Preparations.*

Besides the cases just described, which we have and still are treating in Colney Hatch, I can speak from personal experience of the great change and benefit which I have seen in several others thus treated.

I am able to add a few short notes of one or two cases that have not yet been published.\* The first of these is particularly interesting on account of the patient's family history, where close relatives were affected either with insanity, imbecility, or Graves' disease. For these notes I am indebted to Dr. A. Maude, of Westerham, who is the author of several papers on Graves' disease. In the second case the patient herself had been the subject of this disease only a short time previously. Dr. Wilkin Stabb, of Torquay, kindly sent me the notes. In connection with the subject of Graves' disease, it may be mentioned that Dr. Duke's† patient had a goitre on the right side, and Dr. Putnam's second case‡ had an enlarged thyroid, and suffered from tachycardia, but had no exophthalmos. In the latter case we are told that the thyroid decreased in size with the rapid improvement that took place, and also that there was a strong history of myxœdema in the family.

I.—Mrs. J., a labourer's wife, aged 60, has been under the observation of Dr. Maude § since June, 1887. The onset of myxœdema was very gradual, apparently beginning in 1888. In December last the case presented a large number of the symptoms of the disease as given in the Clin. Soc. Report, but the facial change was never very highly marked. She may be described as an early, slow case of myxœdema, whose mental state was that of chronic dementia with suspicions of neglect and conspiracy rather than the usual mental state. She had some chronic arthritis and emphysema, and at intervals attacks of "stupor" had occurred.

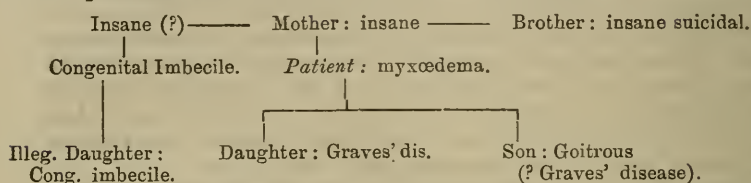
\* In the "Table of Published Cases" it is to be noted that where an asterisk is affixed to a number it indicates that additional information has been added to those cases than is obtainable from the references given. For these extra facts, now for the first time published, I am indebted to the physician whose care the patient was under, and who reported or showed the case in the first instance.

† "Birmingham Med. Rev.," Aug., 1893.

‡ "American Journ. Med. Sc.," Aug., 1893. Dr. Putnam also refers briefly to three cases of acromegalia who were improved by taking thyroids, and he quotes from Drs. Barron and Stattuck that they had used the gland with benefit in simple obesity.

§ The patient was shown at the South Eastern Br. B.M. A. on May 11, 1893. See "Brit. Med. Journ.," May 6, 1893.

The family history of this patient was very neurotic, and may be thus represented :—



Treatment was commenced on December 10th, 1892, by thyroid feeding, raw sheep's thyroids being given pounded as follows:—

Dec. 10	} One thyroid at 11 a.m. The pulse always rose to over 100, and occasionally the patient sweated freely after the dose.
" 14	
Jan. 3	
" 10	
" 17	
" 24	

Feb. 1.—Two thyroids. The patient became very faint and collapsed, and her pulse increased to 130, and became very irregular.

Feb. 7.—Has lost flesh considerably. Skin warm and moist. Mental state improved.

April 1.—Relapsing rapidly.

May 4.—Very lethargic.

May 5.—Treatment was begun with Burroughs and Wellcome's tabloids. Two tabloids, representing 5grs. each, every day, and continued for ten days.

With regard to the ill-effects, both the raw glands and the tabloids produced great occipital headache, faintness, and a general sense of discomfort, but the former alone caused sickness. The arthritis, which was always of a slight and passive form, with no marked articular effusion and pain, but great knottiness and thickening of the fingers, was not affected by the treatment (as in my case of M. B.). The pain produced by the thyroid extract was not in the joints, but apparently a general muscular pain. As regards the occipital pain, an exceedingly common symptom, Dr. Maude remarks that it does not seem to be superficial, and suggests that it is probably due to distension of the torcula and sinuses at the back of the skull.

Dr. Maude will not express a decided opinion as to whether his patient was insane apart from the myxœdema or whether insanity pre-existed, as the onset of the mental state and the swelling, etc., were both so gradual. He says that he had an impression quite two years before he made up his mind that she had myxœdema, that she had primary dementia, but he goes on to remark that primary dementia in a woman of that age is unlikely, it being more likely that the dementia was myxœdematous all along.

Although the improvement that has so far occurred in the patient's condition was not as marked as in many that have been reported, yet her mental state is much improved. "She can now (Aug. 10) work in the house, keep up a sustained conversation on simple matters such as the weather, her health, or the conduct of her neighbours, and has no delusions at all, though she remains very grumbling and complaining. A point worth noting is that as she improves under treatment she acquires more of that fatuous bonhommie which myxœdematous people often have."

Pilocarpin had previously proved a complete failure.

II.—A female (spinster) aged 22, who has been under the care of and been treated by Dr. Wilkin Stabb,\* had had exophthalmic goitre for eight years. This, however, disappeared after an attack of measles, and was followed by the slow development of a condition which was diagnosed by Dr. Ord in December, 1891, as that of myxœdema. The symptoms of this latter probably commenced in the beginning of 1890. Dr. Stabb commenced treatment on December 20, 1892, and is still continuing it in a modified form. At first he gave half a gland (one lobe) twice a week, coarsely minced and covered with port wine and water,  $2\frac{1}{2}$  hours after a meal. On three occasions a whole gland was given at a time, and once she had four glands within seven days. Sometimes treatment was omitted for a few days, and tonics given in place of the thyroids, on account of a feeling of malaise and rapidity of pulse. The patient is now (August 5) taking "White's powders," being equivalent to  $\frac{1}{3}$  gland once a week.

The results obtained so far are briefly thus:—The skin acted slightly after the first, and freely after the second dose. As regards weight, the patient lost  $13\frac{1}{4}$  lbs. in just a month, but has regained it since. Her pulse rose from 70 to 100 and 120, speech became normal, lips thinned, hair less dry, malar flush departed, and she ceased to feel cold. The temperature, which before treatment varied irregularly between  $94^{\circ}$  and  $97^{\circ}$ , was the last symptom to show any definite improvement, but it is now always above  $97^{\circ}$ , and is generally about  $98^{\circ}$ . She seems now to be a healthy person. The only ill-effect noticed was an increased lassitude during the first month of treatment.

III.—Dr. A. Barron says of his first patient,† after having the juice of half a sheep's thyroid subcutaneously once a week for four months, that she appeared to have returned to her normal condition, and that her weight fell from 12st. 7lb. to 10st. 2lb. The treatment was begun in May, 1892, and now (August 10, 1893) she appeared to be perfectly well, and has a fairly respectable head of hair. There have been no ill-effects. The injections

\* Who referred to the case at the South Western Br. B.M. A. on April 13, 1893. See "Brit. Med. Journ.," May 6, 1893.

† "Brit. Med. Journ.," Dec. 24, 1892.

have been given up, and in their place the patient takes six Burroughs and Wellcome's tabloids every Sunday.

IV.—Mr. William Dobbin says that his case, who was referred to in the "*Brit. Med. Journ.*,"\* was a female of about 40 years of age, with myxœdema of from four to five years' duration. For about six months he prepared an extract of the thyroid according to the formula of Dr. G. Murray, and administered it twice a week hypodermically. After trying minced raw thyroid, which, however, could not be borne as it produced diarrhœa, he used the juice prepared after Hector Mackenzie's method, viz., thyroid macerated in tepid water, strained through muslin, and given in beef tea. Lately tabloids of Burroughs and Wellcome, three twice a day, have been substituted. There have been no ill-effects, except once there was an abscess after injection.

The result has been that the swelling has diminished, unsteadiness of gait removed, and very fair health recovered. The patient can now (August 10, 1893), after about thirteen months of treatment, attend to her domestic duties; she enjoys life, and considers herself well.

Dr. Mackenzie has informed me that amongst cases he has seen treated, in one, that of an old lady, where the disease was of old standing, very little improvement took place, but there was really very little amiss with the patient. In another case improvement was only partial, and although the swelling disappeared and the hair grew, the patient remained very feeble. He adds that "in every case the mental improvement has been unquestionable."

Dr. Arthur Davies, who has had considerable experience with the new treatment, has kindly sent me the following brief notes of the seven cases of myxœdema whom he has treated by thyroid extract given hypodermically and by feeding with dried thyroid powder or tabloids. As will be seen from the "*Table of Published Cases*," most of these have been shown or described elsewhere, but in these notes there is contained some additional information of interest, and at the same time they are brought up to date (Aug. 10, 1893). We thus know the present condition of the patients.

I.—G. W., male, married, age 43; duration of disease 12 years. Treated by hypodermic injections of thyroid extract. Improvement very remarkable after three months, and the patient was scarcely recognizable. Tendency to relapse after six weeks' interval, but again improved under treatment. No bad effects whatever. Under treatment one and a half year.

II.—Alice A., married, age 46; duration seven years. Greatly

\* "*Brit. Med. Journ.*," Feb. 4, 1893.

improved after three months' treatment by hypodermic injections. Tendency to relapse after five weeks' cessation, then put on tabloids and improvement again marked. No bad symptoms. Under treatment one year.

III.—Ada B., single, age 47; duration six years. Treated by thyroid powders. Very great improvement and patient hardly recognizable. No tendency to relapse after five weeks. Rapid loss of weight—four stone in 10 weeks. Under treatment seven months.

IV.—Joseph M., married, age 45; duration five to six years. Treated with thyroid powders. Very marked improvement and patient not recognizable. All trace of myxœdema was gone in three months. No bad symptoms. Under treatment seven months. No tendency to relapse as yet.

V.—May B., married, age 59; duration 10 years. No trace of myxœdema after three months' treatment by thyroid tabloids. No bad effects. Tendency to relapse after six weeks, but again improved under treatment. Total time of treatment seven months.

VI.—Alice T., married, age 54; duration four years. Improved markedly after taking thyroid tabloids. Under treatment four months.

VII.—Susan P., age 43; duration eight years. Improved at first for six weeks under injections. Patient lost sight of for two months, then put on thyroid tabloids and again improved. Under treatment on and off for 16 months.

### *Comparison of the Various Methods : General Conclusions.*

There can be no doubt as to the advantages which the thyroid treatment holds over every other drug or mode of treatment in this disease, and in conclusion it only remains to say a word or two as to the best method of administering this new but powerful remedy.

Already I have passed in review with more or less fulness the various methods that have been proposed. They may be summarized as follows :—

1. Thyroid grafting.
2. Subcutaneous injection of an extract of the thyroid gland.
3. Ingestion of an extract (aqueous or glycerine) of the thyroid gland.
4. Ingestion of thyroid gland, raw or slightly cooked.
5. Ingestion of a dry extract obtained from the thyroid gland, in the form of a powder, tabloid or capsule, or pill.
6. Ingestion of thyroïdin.

Of thyroid grafting I think I have said sufficient to show that so far the results obtained have, in a manner, been disappointing and scarcely what at one time was hoped of it. They have certainly not been followed by the same striking results as those ensuing from the more recent methods adopted. At the same time considering the fact that the treatment by these latter is not a permanent cure, and that the drug has to be taken at certain intervals in order to maintain the improved condition brought about (a fact which is easy to understand), it would seem that our only hope of a permanent cure for myxœdema lies in some method by which transplantation can be brought to greater perfection and the graft made capable of living in its new position. Professor Horsley, at Newcastle, has lately called attention to this when he said \* that "it would appear more reasonable to perform transplantation after a prefatory treatment by feeding or injection so as to provide that the grafted gland should be embedded in normal connective tissue and not in diseased tissue."

By the injection of a fluid extract subcutaneously the treatment became at once more simple and free from the many risks of a large operation. It was a small operation that no physician would mind undertaking, and its immediate effects were much more striking. Moreover, it has been shown that the cure could be maintained by the occasional use of a smaller amount than that first employed, and the ill effects that followed its use in many of the earlier cases have been shown to be much lessened or avoided by the more careful use of the fluid and by paying greater heed to the regulation of the dose, and to the subject on whom it was being used.

A watery or a glycerine extract appears to be equally efficacious, and either can be made without a great amount of trouble, although it is perhaps better to obtain it at regular intervals from some druggist of repute, several of whom now supply it at a moderate cost.

With regard to the best dose to employ this would depend on circumstances, such as the age of the patient, duration of the disease, and various other small points that can only be decided in individual instances. Dr. Murray, at the Clinical Society, said he now injected about  $\text{mxxv}$ . at a time, very slowly, which caused less irritation than a larger dose,

\* Report of Annual Meeting of Brit. Med. Assoc. at Newcastle-on-Tyne, "Lancet," Aug. 5, 1893,

and in order to maintain the patient in health he recommended the use of a much smaller dose.\* In this latter, which he called the second stage of the treatment, he had also given the extract by the mouth—daily doses of *m*x. given in water—and on another occasion † “he urged a small dose daily rather than a large dose at longer intervals.”

Although the ingestion of thyroid glands, whether raw or slightly cooked, appears perhaps the simplest method possible, it certainly is not without drawbacks. The principal of these is the difficulty of giving a fixed dose. In some cases in which this method has been employed bad symptoms have followed. And as the thyroid glands vary greatly in size, not only in different animals, but also in the same species,‡ and probably also vary in their activity with the age of the animal and other circumstances, if the patient be allowed to procure the gland themselves their eating may be followed by results of a very unfavourable nature. It is essential, therefore, that when used they should be ordered by the medical attendant, and whilst being employed the patient should remain constantly under his observation. When the raw glands are given they should not be more than one lobe of the thyroid two or three times a week, as recommended by Drs. Pasteur and Calvert.§

Dr. Hector Mackenzie does not now allow the raw gland to be eaten, as it has given rise to gastro-intestinal symptoms, but gives his patient a freshly-made extract. Writing with regard to his first case, in a private letter on May 5th, he said, “My patient is keeping very well. I don’t think anyone seeing her now would suspect her to be a case of myxœdema. In fact, within a few weeks of the commencement of the treatment the characteristic appearance of symptoms had disappeared. She continues to have a freshly prepared liquid extract of the gland once a week. She comes up to the hospital where the nurse prepares the extract for her, simply mincing it up finely, letting it stand for a time in some beef tea and then straining. The catamenia have lately returned after an absence of five years.”

\* “Lancet,” Feb. 4, 1893, p. 248.

† “Brit. Med. Journ.,” Feb. 25, 1893, p. 411. See also Dr. Murray’s illustrated paper on “The Treatment of Myxœdema and Cretinism,” “Lancet,” May 13, 1893.

‡ See “Lancet,” Feb. 4, 1893, p. 274.

§ “Clinical Society,” Jan. 27, 1893; “Lancet,” Feb. 4, 1893.

Again, on August 5, he says that his "original patient" was in very good health and there were no signs of myxœdema whatever. Lately she has been having the expressed juice of a whole thyroid gland once a week, and occasionally "White's thyroid powders" were substituted (three a week, the equivalent of half a gland). She, however, preferred the fresh extract.

The use of the extract in the form of a powder is a distinct advantage in several respects. It is a grey tasteless powder which will keep good for a sufficient period. It can be given in a variety of vehicles. It is prepared in a scientific way,\* so the dose can be accurately measured. The results from its employment have been as satisfactory as those otherwise obtained. Or, if preferred, tabloids prepared by compressing the powder can now be obtained, each being equivalent to five grains of the fresh thyroid.† They have received considerable favour.

Dr. Arthur Davies wrote me under date May 9th:—"As regards the cases I have treated solely by giving the dried thyroid extract, each one is still in a vastly improved state; indeed, one may now say that there is no sign or symptom of myxœdema in them. I am keeping up the treatment, but by degrees gradually lessening the frequency of the dose. I formerly gave White's powders, but now use Burroughs and Wellcome's tabloids, which I find equally efficacious, though perhaps slower in action. Of course, as regards rapidity of treatment, the subcutaneous injection is the most quick." Whichever way is preferred, the rapidity of the recovery appears to depend upon the amount of the extract employed. It is possible, however, that by giving the extract in smaller quantities over a longer period that a less rapid recovery will be found to be more beneficial to the patient, and lead to a more lasting improvement.

At the time when the drug is exerting its power most actively the patient often feels weakened and out of sorts, and it is then that the use of tonics in combination with the new treatment, as suggested by Dr. McCall Anderson,‡ is not amiss, and may be employed with advantage. Nitro-

\* Each powder representing the sixth part of a sheep's thyroid as supplied by Mr. Allen, and 60 grains of the powder being equivalent to one fresh gland as supplied by Ferris, of Bristol. The latter firm also make the powder up into capsules.

† Prepared by Messrs. Burroughs and Wellcome. See "B. M. J.," April 1 p. 701.

‡ "The Treatment of Myxœdema," "The Practitioner," Jan., 1893.

glycerine, too, has been found by Mr. C. J. B. Johnson to "promptly relieve the headaches which came on when the thyroid was freely given."\*

I will now quote from a letter I received from my friend Dr. Murray on the 7th May, in which he gives the latest conclusions as regards treatment at which he has arrived. "The treatment consists of two stages—first, removal of symptoms; second, maintaining improved condition. The first stage can be carried out by injections or by the mouth. If injections are used not more than  $\text{m}\chi\text{v}$ . at a time should be injected, as larger doses are apt to cause irritation. Injections may be repeated two or three times a week. If given by the mouth it is best to start with a daily dose of about  $\text{m}\chi$ .; if not sufficient give it twice. If there is undue acceleration of the pulse diminish the dose. In the secondary stage it is best to give by the mouth, and give the smallest daily dose which keeps the temperature normal or above  $97^{\circ}$ . I find my original glycerine extract, with carbolic omitted, made by Brady and Martin, most satisfactory to give by the mouth.  $\text{ziss.}$ —one whole sheep's thyroid."

Writing to me again a few days later (May 14th) with regard to his first case—that which has borne the test of time the longest—he says:—"My first case has now no symptom of myxœdema left, and is as well as she could be, both in mind and body, leading an active life as a working man's wife. She takes regularly  $\text{zj}$ . of the thyroid extract each week in daily  $\text{m}\chi$ . doses. As it is now more than two years since the treatment was first started I think we can fairly conclude that the improvement may be maintained indefinitely." He also stated, concerning the patient whose photo was reproduced in the "*Brit. Med. Journ.*," August 27, 1892, that she was kept in the improved condition by a daily dose of  $\text{m}\text{v}$ . of the extract, and that the photograph taken a year ago represents the present condition very well, except that some of the hair is now seven inches long.

In conclusion, I will quote a remark of Dr. Murray's with which I feel sure many will agree. "If all cases of myxœdema are put on the treatment as soon as diagnosed the insanity of myxœdema ought to cease to exist, and if cretins are fed on some thyroid preparation from youth up they should develop into more useful members of the community." I think it is the duty of all, who in future have the opportunity, to test the truth of what has been said regarding

\* "*Brit. Med. Journ.*," May 6, 1893, p. 955.

this new and wonderful remedy, one which has rightly been said to be "one of the greatest therapeutic triumphs of the age."\*

#### REFERENCES.

Reproductions from photographs of patients who have undergone the thyroid treatment may be found in the following journals:—"Brit. Med. Journ.," Aug. 27, 1892; Jan. 14, 1893, p. 64; April 8, 1893, pp. 737 and 738. "Glas. Med. Journ.," Sept., 1892. "Clin. Soc. Trans.," Vol. xxv., 1892. "Lancet," May 13, 1893. "Sheffield Med. Journ.," July, 1893, etc.

I have to acknowledge my indebtedness to Drs. Murray, Davies, and Mackenzie for the use of some excellent photographs showing myxœdematous patients before and after treatment by the thyroid, which were shown at the meeting of the Medico-Psych. Assoc. on May 18th, 1893.

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*For Tables see Appendix.*

#### CLINICAL NOTES AND CASES.

*Hypertrophy of Scalp.* By GEORGE FOY, F.R.C.S., Dublin.

Dr. McDowall will find a case of extraordinary development of the scalp reported in John Bell's article "On the Unlimited Growth of Tumours," which is reprinted in his "Principles of Surgery," Vol. iii., 4to., 1808 A.D., published by Longman, Hurst, Rees, and Orme, London. The book is now scarce, and the case is so remarkable that I give a summary of it.

Eleanor FitzGerald, a native of Ireland, born in the

\* "Lancet," Feb. 4, 1893.